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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/580,130

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Karin A. Eidne

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EXAMINER

SNYDER, STUART

ART UNIT

PAPER NUMBER

1648

NOTIFICATION DATE

DELIVERY MODE

11/16/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/580,130	<b>Applicant(s)</b> EIDNE ET AL.	
	<b>Examiner</b> STUART W. SNYDER	<b>Art Unit</b> 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 June 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 3,7-9,11-20,22-36 and 46 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3,7-9,11-20,22-36 and 46 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                            |                                                                                         |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

## DETAILED ACTION

### *Status of the Claims*

1. Acknowledgement is made of cancellation of claims 1, 2, 4-5, 10, 21 and 37-45; amendment of claims, 11, 12, and 18-20 as well as addition of new claim 46. Claims 3, 7-9, 11-20, 22-36 and 46 are pending and examined herein.

### *Specification*

2. Objection to the specification because of incorrect reference to Figures 2 and 3 entities in the Brief Description of the Figures is **withdrawn** in view of amendment of the specification in Applicants' filing of 6/5/2009.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Rejection of claims 3, 7-9, 16 and 18 under 35 U.S.C. 102(b) as being anticipated by Balasubramanian, et al. is **maintained**. The claims, as amended on 6/5/2009, are drawn to a multi-component detection system comprising three fluorescently tagged groups capable of interacting with each other. Applicants traverse the rejection and have amended claim 3 to recite that external stimuli are applied directly or indirectly to modulate the association of interacting groups and state that "Balasubramanian does not teach or suggest [this] aspect". However, looking to the specification to determine the meaning of the term

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“external stimuli”, paragraph 55 elaborates “stimuli are reagents including any known molecule...nucleic acid”. Thus, a nucleic acid, including polynucleotides, may serve as “external stimuli”. Figures 1 and 2 of Balasubramanian, et al. clearly depict three labeled polynucleotides that are capable of interacting with each other only in the presence of a target polynucleotide—an external stimuli. Figure 1 of Balasubramanian, et al. depicts the interaction of three tagged polynucleotides which are capable of FRET interaction in which the fluorophore F is capable of FRET with either fluorophores X and Y if in the presence of the target strand and appropriate stimulation of fluorophore F. Furthermore, Figure 2 of Balasubramanian, et al. depicts stimulation of FAM which is capable of stimulating ROX or TMR if excited by an appropriate light source at 488 nm and if the FAM labeled nucleotide is bound to the target sequence as well as at least one of the other tagged nucleotides. Thus, Balasubramanian, et al. teaches each and every limitation of claims 3, 7-9, 16 and 18.

4. Rejection of claims 3, 7-9, 16, 18 and 20 under 35 U.S.C. 102(b) as being anticipated by Liu and Lu is **maintained** for reasons of record and the following. The claims, as amended on 6/5/2009, are drawn to a multi-component detection system comprising three fluorescently tagged groups capable of interacting with each other. Applicants traverse the rejection and have amended claim 3 to recite that external stimuli are applied directly or indirectly to modulate the association of interacting groups and state that “Liu and Lu does not teach or suggest [this] aspect”. However, looking to the specification to determine the meaning of the

term “external stimuli”, paragraph 59 (Page 22) elaborates “stimuli are reagents including any known molecule, organic or inorganic”. Thus, metallic entities including zinc, may serve as “external stimuli”. Figure 3 and the accompanying text of Liu and Lu clearly depict triply-labelled polynucleotides that are capable of interacting with each other differentially in the presence of an ionized zinc—an external stimulus (see page 15212). Such differential interaction is further discussed throughout the Results section (pp 15212 ff) and is hypothesized to reflect bending of the different arms of the so-called DNAzyme (see especially figures 4 and 5). Thus, Liu and Lu teaches each and every limitation of claims 3, 7-9, 16, 18, and 20.

5. Rejection of claims 3, 7-9, 16 and 18 under 35 U.S.C. 102(b) as being anticipated by Kumar, et al. (WO 2004/029579) is **withdrawn** in view of amendments to the claim.
6. Claims 11, 12, and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by both Balasubramanian, et al. and Liu and Lu. Claims 11 and 12 are drawn to the system of claim 3 and characterize the nature of the external stimuli, especially to include various organic and inorganic stimuli as well as changes in physical or chemical conditions; claim 46 limits the energy of the activated tags to include resonance energy and/or light energy. Figures 1 and 2 of Balasubramanian, et al. clearly depict three labeled polynucleotides that are capable of interacting with each other only in the presence of a target polynucleotide—an external stimuli. Figure 1 of Balasubramanian, et al. depicts

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the interaction of three tagged polynucleotides which are capable of FRET interaction in which the fluorophore F is capable of FRET with either fluorophores X and Y if in the presence of the target strand and appropriate stimulation of fluorophore F. Furthermore, Figure 2 of Balasubramanian, et al. depicts stimulation of FAM which is capable of stimulating ROX or TMR if excited by an appropriate light source at 488 nm and if the FAM labeled nucleotide is bound to the target sequence as well as at least one of the other tagged nucleotides. Figure 3 and the accompanying text of Liu and Lu clearly depict triply-labeled polynucleotides that are capable of interacting with each other differentially in the increase of an ionized zinc—an external stimulus (see page 15212)—concentration from 0 to 1 mM. Such differential interaction is further discussed throughout the Results section (pp 15212 ff) and is hypothesized to reflect bending of the different arms of the so-called DNAzyme (see especially figures 4 and 5); figure 4 explicitly teaches increased FRET dependent on increasing  $\text{Zn}^{2+}$  concentration. All of the figures and accompanying text teaches FRET, a type of resonance energy transfer ultimately leading to visible light energy from the second or third fluorophore. Thus, the limitations of claims 11, 12 and 46 are taught by each of Balasubramanian, et al. and Liu and Lu.

7. Claims 24-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Kissa, et al. (In Vivo Neuronal Tracing with GFP-TTC Gene Delivery. *Molecular and Cellular Neuroscience*. 2002; 20:627–637). The claims are drawn to a DNA construct, vectors comprising the DNA construct, and cells containing the DNA

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construct wherein the DNA construct comprises an “interacting group and tag” encoding polynucleotides. Kissa, et al. teaches a plasmid vector and an adenovirus vector infecting neuron comprising green fluorescent protein (GFP) fused to tetanus toxin C-fragment (TTC); GFP serves a tag to allow detection of the fusion protein by fluorescence whereas TTC specifically targets the fusion protein to neuronal cells, e.g. an interacting group. Thus, Kissa, et al. teaches each and every limitation of claims 24-36 and the claims are properly rejected under 35 U.S.C. 102(b).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Rejection of claims 3-20 and 22-36 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **withdrawn** in view of Applicants' arguments and amendments filed 6/5/2009.
9. Claims 7-9, 13-17, and 23-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 7, 8 and 23 recite the limitation "the interacting group" in the first line; claim 9 depends on claim 7 and claims 24-36 depend on claim 23; and claim 13 recites "the detection tag" and claims 14-17 depend on claim 13. There is insufficient antecedent basis for this limitation in the claims. Each of claims 7, 8, 13 and 23

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depend on claim 3 which recites at least three different “interacting groups” and three different “tags” but no “detection tags”. Thus, in the first instance it is unclear which of the three “interacting groups” are referred to in claims 7, 8, 13 and 23; and in the second instance there is no antecedent basis for the term “detection tag”.

### ***Claim Objections***

10. Claims 24-36 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims depend on claim 23 which is drawn to a fusion protein comprising an interacting group and a tag. Claims 24-36 are drawn to DNA encoding such a fusion protein and do not further limit the nature of the fusion protein.

### ***Conclusion***

11. No claims are allowed.
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to STUART W. SNYDER whose telephone number is (571)272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mary E Mosher/  
Primary Examiner, Art Unit 1648

Stuart W Snyder  
Examiner  
Art Unit 1648

SWS